GENDER-RELATED SEROTONIN SYSTEM FUNCTION AND PTSD RISK

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Abstract

Background: Research suggests that the serotonin (5-HT) system potentially plays an important role in the behavioral dysregulation of PTSD. There is evidence that gonadal hormones, menstrual cycle phase, and reproductive state affect serotonin system function. This suggests that gender-related differences in 5-HT system function could contribute to the well-documented increased vulnerability to PTSD in women. The knowledge of specific mechanisms by which this could occur could guide development of interventions to reduce PTSD risk in women.

Method: A PubMed search was conducted to find relevant studies published on gender, the neurobiology of PTSD, and the serotonin system. Other relevant studies or reviews referenced in those articles were also examined.

Results:

Published research with regard to serotonin synthesis and receptor levels suggests that there are:

- Decreased baseline rates of serotonin synthesis in the brains of women compared to men, as well as greater decreases in brain serotonin synthesis after tryptophan depletion. (Nairzawa et al., 1997).
- Widespread increases in cortical serotonin 2A receptor availability after hormone therapy in eugenic postmenopausal women. (Moses-Kolka et al., 2003).
- The number of serotonin transporters in the frontal lobe and brainstem is increased by estrogen in rns. (McQueen, Summer et al., 1999).
- Thus, it is possible that the effects of the serotonin transporter gene variant are influenced by gender or gender-related hormones.
- Increased Bmax for [3H]paroxetine binding in the late follicular phase than in the ovulatory phase, early luteal phase and mid-luteal phase. (Whitbeck AC 2004).
- Increased Bmax for [3H]-I5D3 binding in the early follicular phase and the early luteal phase compared to the mid-luteal phase. (Whitbeck AC 2004).

Conclusions:

- Decreased serotonin synthesis in women during stress (which increases demand for 5-HT synthesis and release), combined with menstrual phase associated estrogen upregulation of frontal lobe 5-HT2A receptors, and possession of particular 5-HTTLPR risk alleles may compromise frontal lobe function.
- Research suggests that this could dislocate the amygdala and enhance fear conditioning or impair with extinction, thereby increasing PTSD risk in women.
- Clinical translational studies (combined imaging, genetic, and psychological, psychopharmacologic challenge paradigms) can be designed to test these hypotheses.

Methods:

A PubMed search was conducted to find relevant studies published on gender, the neurobiology of PTSD and the serotonin system. Other relevant studies or reviews referenced in those articles were also examined.

Published research with regard to the serotonin transporter gene: (Biver, 1996).

- The genetic locus of interest involves a polymorphic region of the serotonin transporter gene (5-HTTLPR). The gene itself exists as several alleles.
- The effect of stressful life events on depressive symptoms in young adults significantly stronger among SS or SL subjects than among LL subjects exhibited by a greater activation of the amygdala in response to fearful stimuli. (Wurtz et al., 2005).
- There are interactive effects of gender and 5-HTTLPR on mood and impulsivity during tryptophan depletions in healthy people. Women report mood reduction while men showed impulsive response style. (Woldehagen E et al., 2007).

- Increased mood reduction is seen in women with the LL and S/S polymorphism.

Published research with regard to the serotonin transporter gene: (Biver, 1996).

- There may be a decrease in serotonin availability at baseline in PTSD in both men and women, accompanied by an upregulation of postsynaptic 5-HT-2 receptors.
- Women may be more vulnerable to anxiety associated with stress-induced increases in endogenous serotonin acting at upregulated 5-HT-2 receptors.
- Decreased serotonin synthesis in women during stress (which increases demand for 5-HT synthesis and release), combined with menstrual phase associated estrogen upregulation of frontal lobe 5-HT2A receptors, and possession of particular 5-HTTLPR risk alleles may compromise frontal lobe function.
- SS phenotype may be a protective factor dampening depressed mood in women experience in response to reduced 5-HT transmission.

References: